

Medical Staff Conference

Evaluating and Treating Intractable Cough

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California, San Francisco. Taken from transcriptions, they are prepared by Drs Homer A. Boushey, Associate Professor of Medicine, and David G. Warnock, Associate Professor of Medicine, under the direction of Dr Lloyd H. Smith, Jr, Professor of Medicine and formerly Chair of the Department of Medicine. Requests for reprints should be sent to the Department of Medicine, University of California, San Francisco, School of Medicine, San Francisco, CA 94143.

DR SMITH:* *The topic will be "Evaluating and Treating Intractable Cough," a rather intriguing title, and Dr Michael Stulbarg will give this presentation. Dr Stulbarg is Adjunct Associate Professor of Medicine and Chief of the Chest Clinic here.*

DR STULBARG:† Thank you, Dr Smith, ladies and gentlemen. Many patients seek medical care for the complaint of cough. In 1979 about 13 million people saw their physicians for evaluation of cough and, in fact, cough was the second most common reason given for seeing a physician. Most of these coughs are self-limited, but in a few persons the coughs are persistent, worrisome and sometimes even disabling.

I would like to begin with the report of a case that we recently labored over for several months. I think this case emphasizes the complex and at times frustratingly prolonged evaluation necessary to achieve a specific diagnosis for a patient with intractable cough. I shall then turn to the physiology of cough, the complications of cough (because these are what often bring a patient to a physician's attention), the diagnostic approach to cough, including the long differential diagnosis, and finally to treatment.

Report of a Case

The patient, a 30-year-old housewife from Manteca (California), was referred because of chronic cough of three to four years' duration with worsening over the past year. The cough began insidiously during pregnancy and had persisted since that time. She noticed that it increased with exertion, but she could relate it to no other factors such as position, time of day or meals. She also complained of a chronic "tickle" in her throat possibly related to postnasal drip and of occasional ill-defined episodes of "choking" both day and night. She had been seen by several physicians who had given empiric trials of antibiotics and steroids with no benefit. Codeine gave considerable relief, preventing her posttussive emesis and reducing the disruption of her sleep.

Past history of pertinence included drainage of a right frontal sinusitis and nasal septoplasty. She said she had no

allergies or occupational exposures. One sister had hay fever. Although review of systems elicited a variety of nonspecific complaints, the most intriguing symptom was that of occasional difficulty swallowing solids but not liquids.

On physical examination she was mildly obese and had an occasional dry cough. Vital signs were normal. There was no inflammation of either tympanic membrane and no hairs impinging upon them. There was no boggiess, erythema or polyps of the nose, and the oropharynx was without cobblestoning or visible mucus. The neck was free of masses and the trachea was freely mobile. Her lungs were clear to percussion and auscultation. On cardiac examination there were a palpable pulmonic component of the second heart sound and a grade 2/6 systolic ejection murmur.

Several studies had already been done, the results of which were unrevealing; these included a hemogram, chemistry panel, chest x-ray films, allergy skin testing, bronchoscopy, esophagoscopy and otolaryngologic consultation. Because her evaluation had been so detailed, I was concerned that she might have one of the uncommon causes of cough such as interstitial lung disease or, because of her cardiac findings, occult heart disease. Further workup included a new chest film, which was normal, pulmonary function studies, the results of which were normal except for high flow rates (a finding of questionable significance), and echocardiogram, which showed mitral valve prolapse with normal left ventricular function. A gallium lung scan, done in the search for occult interstitial lung disease, was minimally and probably insignificantly abnormal. To determine whether the patient might have airway hyperreactivity characteristic of asthma, a histamine challenge test was done and was within normal limits.

Because the results of these studies were unrevealing, she then underwent noninvasive exercise testing looking for clear-cut cardiac or pulmonary dysfunction. Oxygen uptake and minute ventilation were measured in response to incremental exercise. Results of the test showed greatly abnormal exercise tolerance for a 30-year-old woman, with abnormal ventilatory and cardiac responses. Repeat exercise testing with measurement of arterial blood gases and wasted ventilation was technically inadequate but did confirm the results of

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ABBREVIATIONS USED IN TEXT

CT = computed tomographic [scan]

FEV₁ = forced expiratory volume in one second

the prior study. Because of the unexplained abnormal findings on exercise testing, cardiologic consultation was sought and the clinical assessment showed no abnormalities. She then underwent cardiac catheterization. As the results were normal, I discharged her with the hope that she would feel reassured that we had done "everything." However, she called a few weeks later still distressed because of persistent coughing, especially at night. She was readmitted to hospital with the hope that the house staff would come up with something that I had missed. Her laboratory values and chest film were still normal. The house staff suggested the possibility of psychogenic cough. The psychiatrist who evaluated her felt that she was mildly depressed and that the cough could be due to a conversion reaction.

At this time the complaints of dysphagia and occasional substernal discomfort began to draw our attention. Because of these complaints, she was instructed to maintain the head of her bed at 30 degrees of elevation both day and night. This seemed to be associated with a decrease in her cough, suggesting the possibility of esophageal disease. A barium swallow study was therefore done and the findings suggested the presence of a mass impinging on the esophagus. However, a computed tomographic (CT) scan of the chest was normal. Because these studies did not exclude esophageal reflux or esophagitis, esophagoscopy was done. Results of the study showed that she did in fact have distal esophagitis and antritis. Treatment with antacids and cimetidine led to a pronounced improvement in her cough, but it was not until a few months later when metoclopramide hydrochloride was added to her regimen that her cough actually *disappeared*.

I apologize for presenting this case at such length, but I wanted to emphasize both the effort and the satisfaction of reaching a specific diagnosis.

Physiology of Cough

Cough may be a voluntary event or an unsuppressible reflex.¹⁻³ It may result from stimulation of irritant or rapidly adapting receptors by mucus or environmental irritants.² These receptors are present throughout the respiratory tract from the upper airway including the nose, sinuses, oropharynx and larynx to the lower airway including the trachea and the carinae, both the main carina and the more distal divisions or subcarinae.¹ Following stimulation of these receptors, there is a sudden inspiration, followed in turn by the compressive phase. This phase is marked by tightening of the chest and abdominal muscles against a closed glottis, with a rise in pleural pressure to between 100 and 300 mm of mercury.⁴ At some point, not well defined, the glottis suddenly opens, allowing the rapid noisy exhalation we call a cough. Because of the high intrathoracic pressure that has developed, there is considerable narrowing of the proximal airways and very high linear velocities, resulting in more effective expulsion of mucus or foreign materials than is produced by simple exhalation. The dramatic decrease in the cross-sectional area of the trachea may result in linear velocities in excess of three quarters the speed of sound.⁵

Complications of Cough

It is often the complications of cough that bring a patient to medical attention. The devastating personal distress and social isolation sometimes produced by severe chronic cough are frequently unappreciated. Many patients restrict their social lives and refuse to go to restaurants, theaters or public gatherings because of the embarrassment they experience from their cough. Disruption of family life is a common complaint. The patient who first piqued my interest in chronic cough was a woman whom I was asked to see in the intensive care unit. She had nearly successfully killed herself on two separate occasions because of the impact of an unremitting cough on her marriage.

More common complications include sleep disruption; musculoskeletal, chest or abdominal wall pain; emesis, and syncope.^{1,6-15} The mechanism of emesis is not clear, but it is thought to be related to irritation of the oropharynx. Syncope, a particularly dangerous complication of coughing, may be due either to the effect of increased pleural pressure transmitted directly to the cerebrospinal fluid or to the Valsalva-like effect of increased intrathoracic pressure on venous return and the resultant hypotension.¹¹⁻¹⁵ The mechanical stress of coughing may cause elevations of creatine phosphokinase levels¹⁰ as well as result in fractures of ribs.¹⁶ The cough-induced tearing of abdominal muscles may mimic a ruptured abdominal viscus, and on rare occasions patients have actually undergone an unnecessary operation.⁶⁻⁹

Less common complications of cough include pneumothorax, mediastinal emphysema, pneumoperitoneum¹⁷ and headache.¹⁸ Though poorly documented, other rare complications noted in the past have included fatigue, physical exhaustion, anorexia and rupture of subconjunctival nasal and anal veins.¹⁹ In a recent report, bleeding from esophageal varices induced by coughing was documented.²⁰ Though rarely mentioned as a complication,¹⁹ stress incontinence precipitated by coughing has been a not-uncommon reason for referral in our experience.

Diagnostic Approach

In approaching the differential diagnosis of cough, it may be helpful to consider the locations of cough receptors, because disease in any of these sites might elicit cough.¹ These receptors occur in the ears, the nose and sinuses, the oropharynx, particularly around the larynx, the trachea and the bifurcations of the large airways.^{1,2} They do not occur in the periphery of the lung, perhaps explaining why some patients with extensive pneumonia have little or no cough until they begin producing enough mucus to stimulate the more proximal cough receptors. Receptors are also said to occur in the pericardium, the diaphragm and the stomach,¹ though these must be of much lesser importance as cough is not an important symptom of diseases in those organs.

The diseases that may affect these sites are many. In only two studies have the causes of cough been carefully examined (Table 1). One study, reported in 1981 by Irwin and co-workers, is a prospective study of 49 patients presenting to a chest clinic with unexplained cough in a one-year period.²¹ All of these patients had been seen by at least one previous physician and had defied diagnosis for at least three weeks. They developed clinical criteria that included response to specific therapy for each of their diagnoses. The second

study, by Poe and colleagues, was a retrospective review of patients with prolonged coughing (at least two months).²² Their study was based on a review of charts, and the criteria for diagnosis were not as clear as those in the first study.

Particularly impressive in both studies is the high frequency of asthma—38% overall (Table 1). This diagnosis required the finding of obstruction by spirometry or, if none was present, an abnormal response to bronchial challenge.²³ As abnormal bronchial reactivity alone is not sufficient for a diagnosis of clinical asthma, response to specific therapy was also required. Another large group, 21%, had postnasal drip, a somewhat controversial diagnosis.^{24,25} Patients with this problem report the sensation of mucus “dripping” into the throat and the need for frequent clearing of the throat (as opposed to a deeper chest cough).²⁵ Alone, or combined with asthma, postnasal drip accounted for 35% of the cases of cough in the study by Irwin and associates. The nine patients given both diagnoses responded only partially to therapy for one, but completely to therapy for both diagnoses. In total, then, more than 50% of the patients presenting with intractable cough had either postnasal drip, asthma or both.

Another major category in the second study was postinfectious cough. Such patients were not included in the series by Irwin and co-workers, perhaps because most of them would not have been referred or would have been considered asthmatic. In fact, some did have positive response to methacholine stimulation, but we do not know if they responded to bronchodilator therapy. It has been shown that abnormal bronchial reactivity may commonly persist for as long as two months after a viral infection and then resolve without therapy.²⁶ Bronchitis occurred in 12% of the patients, almost always in smokers, and was usually associated with nonreversible airway obstruction. In all of the cases where information was available, cough was greatly improved or disappeared after cessation of smoking, as has been previously reported.²⁷

Esophageal disease represented a small but important minority of cases. The case described would clearly have fallen into this group. This diagnosis required abnormal barium esophagograms, endoscopy showing esophagitis or abnormal results on pH monitoring of the distal esophagus. In the combined series only one patient had cough due to lymphangitic

spread of cancer²¹ and one patient was found to have an endobronchial adenocarcinoma.²² Although cardiac disease was rarely the explanation for chronic cough, in one patient the results of a cardiac catheterization did show left ventricular failure.²¹ Interstitial disease of the lung was the cause of cough in only one patient.²¹ In the retrospective series they could not identify a specific diagnosis in 11 patients, of whom 7 were considered to be of psychogenic origin, though the criteria for this assignment were not described.²²

This list is by no means complete, but it does reflect the most commonly reported causes of cough. Presumably any disease of the lungs or airways may on occasion present with cough. Other unusual causes have been reported. Removing residual sutures from a prior resectional operation resolved cough in one group of five patients.²⁸ Stimulation of the tympanic membrane by hairs in the auditory canal has caused recurrent severe coughing paroxysms that resolve within several days of removing the hair.²⁹ Cases of radiologically occult bronchiectasis³⁰ or an endobronchial nematode³¹ may present with chronic cough. Inhaling toxic substances may seem an obvious cause of cough,³² but patients often deny their regular use of tobacco or marijuana. We have seen several patients whose coughs were due to causes not clearly described previously. Several patients have had cough associated with unexplained dryness of their oropharyngeal mucous membranes. Finally, we have seen one patient with a postoperative neuroma of the glossopharyngeal nerve resulting in a disabling cough elicited by any superficial stimulation of the neuroma, such as touch or inhaling cold air.

Medical History

Though many of these diagnoses seem straightforward, it is evident that patients with intractable cough would not have been referred to a specialty clinic for evaluation if that were so. Irwin and colleagues found that a specific diagnosis could be made by an appropriate history alone 80% of the time.²¹ Several historical points are worth emphasizing.

Identifying precipitating causes or time of onset of cough may be particularly helpful. For example, patients with esophageal problems, heart failure or asthma are more likely to cough at night. Patients with bronchitis or postnasal drip may complain of cough and sputum production early in the mornings. A relationship to meals may suggest esophageal disease. Cough related to interstitial lung disease or asthma often increases with deep breathing or exertion. Identifying exposures to allergens or irritants both at home and at work may relate to cough. A prior history of infections may be important. Viral infections may cause persistent cough for as long as a couple of months following the episode.²⁶ Patients with severe chest infections as children may be more prone to pulmonary disease in adulthood. Bronchiectasis may be clinically silent (dry) for many years and then become symptomatic in adult life following a respiratory tract infection.

Some medications may cause cough. β -Blockers given orally for cardiovascular disease or topically for glaucoma may precipitate asthma. A variety of drugs including chemotherapeutic agents and nitrofurantoin may cause interstitial lung disease. Awareness of a prior response to empiric treatment may be very helpful. Such treatment may have been appropriate, but physicians are reluctant to continue treatment with either steroids or antibiotics without a specific diagnosis.

TABLE 1.—Causes of Persistent Cough

Causes	Studies		Total Patients	Total Percent*
	Irwin et al, 1981 ²¹	Poe et al, 1982 ²²		
Asthma	12	39	51	(32)
Postnasal drip	14	9	23	(15)
Asthma plus postnasal drip	9	..	9	(6)
Postinfectious	..	27	27	(17)
Bronchitis	6	13	19	(12)
Esophageal	5	4	9	(6)
Cancer	1	3	4	(3)
Cardiac	1	3	4	(3)
Interstitial disease	1	..	1	(1)
Psychogenic	..	7	7	(4)
Undetermined	..	4	4	(3)
Total	49	109	158	

*Percentage does not equal 100 due to rounding of numbers.

On review of systems, one should pay particular attention to the much-neglected nose and sinuses. Postnasal drip is an important cause of cough, and therapy is available.^{24,25,32} Interpreting the complaint is sometimes difficult because so many patients complain of "sinus" problems,³² but in those with troublesome cough aggressive treatment of this syndrome may be worthwhile. Airway symptoms are often not fully appreciated. Patients may belittle their chronic sputum production or consider it normal, but sputum production is an important symptom of either chronic bronchitis or chronic rhinitis. Dyspnea, if present, is an important clue to a wide variety of cardiopulmonary disorders. Symptoms of esophageal disease such as heartburn or dysphagia should be looked for specifically.¹³ Knowledge of underlying diseases, such as Sjögren's syndrome, which could affect drying of the mucosa, for example, may be very helpful.

Physical Examination

A thorough physical examination is clearly necessary to separate the many diseases that may cause cough. Irwin and co-workers found it useful 60% of the time.²¹ If a patient does not cough spontaneously, ask for a voluntary cough and listen to the quality of the cough. The cough is "wet" in patients with asthma, bronchitis and postnasal drip and "dry" in those with most of the other conditions. Note if it is a deep chest cough or just clearing of the throat and if it is brought on by respiratory tract maneuvers during the physical examination, such as laughing or deep breathing. On examination of the ears, look specifically for irritating hairs or impacted cerumen. Polyps or boggiess of the nasal mucosa and visible mucus or cobblestoning of the oropharynx (an accumulation of lymphoid tissue that is common in children, but not normally seen in adults) may suggest chronic rhinitis. Other important clues on physical examination would include neck masses or fixation of the trachea, unsuspected crackles or wheezes, cardiac murmurs or gallops, midepigastic tenderness, clubbing or any signs of systemic illness.

Other Studies

Although we rely a great deal on chest roentgenograms for diagnosis, patients with chest diseases may on occasion have perfectly normal chest roentgenograms.³³ Of patients with interstitial lung disease, as many as 16% may have normal chest x-ray films.³³ Endobronchial neoplasm, particularly bronchial adenomas, bronchiectasis, cystic fibrosis, endobronchial tuberculosis and especially foreign bodies may not be radiologically detectable.³³

Our approach to diagnosis begins with a data base that includes history, physical examination, chest film and spirometry. At this point, I would like to focus on what to do when a diagnosis has not been made by this basic approach. If there is sputum, it may be worth examining.³⁴ The finding of eosinophils may suggest asthma, whereas the finding of abundant polymorphonuclear leukocytes and bacterial organisms may suggest chronic bronchitis.

Formal pulmonary function studies including measurement of diffusing capacity and maximal expiratory flow-volume loops may be more sensitive than simple spirometry for early diagnosis of interstitial lung disease, chronic obstructive pulmonary disease and upper airway disease.²⁵ Though not yet widely available, bronchial stimulation with

histamine or methacholine is an important way of identifying abnormal irritability or reactivity of the airways, as occurs in asthma.²³ About a quarter of the cases in the series of Irwin and associates were diagnosed by this technique.²¹ The test measures abnormal responsiveness of bronchial smooth muscle as assessed by the increase in airway resistance or the decrease in the forced expiratory volume in one second (FEV₁) following inhalation of methacholine or histamine. This is a dose-related phenomenon, and people with asthma respond to much lower doses of inhaled drug than do healthy persons. Unfortunately, the test is not perfectly discriminatory as some patients, such as those with allergic rhinitis, may fall into the so-called asthmatic range.²³ Corrao and associates reported the cases of a small group of patients with chronic cough who had no history of dyspnea or wheezing, normal findings on physical examination and normal resting pulmonary functions.³⁵ When tested with inhaled methacholine, they all had a decrease in their FEV₁, whereas none of the controls responded in that way to the same dose. All six of these patients responded to bronchodilator therapy with resolution of their cough. When the drug regimen was subsequently discontinued, the cough returned. This is the most convincing evidence of the cough variant of asthma.

All of the other diagnostic studies are of less common use, and the decision to use them is initially based on the history. A patient with severe persistent cough, such as the one presented here, eventually will undergo most of them. The other studies that were done in this patient including exercise study, gallium scan and CT scan are certainly of much lower yield and are rarely used in the workup of a coughing patient. Psychiatric evaluation has a clear role after extensive medical evaluation.²² It is especially helpful in an adolescent with psychogenic or habitual cough.³⁶ We have seen two teenagers with this dramatic syndrome. Both were shy, had school-adjustment problems and in both cases the cough bothered the parents much more than it bothered the children. As reported previously,³⁵ the critical historical feature was that even though the cough occurred every few seconds during the day, making school attendance impossible, it disappeared with sleep. The cough increased when either nurses or physicians were present. In the first case, the parents unfortunately signed the patient out of hospital when we suggested that there might be a psychogenic cause. In the second case, the patient returned home with our reassurance and instructions to the parents simply to ignore the cough and reassure the child that all would be well. One week after returning home to Florida, upon awaking one morning, she said to her mother, "I don't think I need to cough anymore."

Treatment

Not every patient needs such an extensive workup. If the history is clearly suggestive, response to empiric treatment may be an adequate "test." Specific therapy for most of the diagnoses mentioned is straightforward. A notable exception is postnasal drip or chronic rhinitis. A combination of topical nasal steroids (beclomethasone dipropionate or flunisolide), combined with one of the long-acting antihistamine decongestant combinations, may be dramatically effective.³⁷ If the cause is clearly allergic, topical administration of a nasal solution of cromolyn sodium may be successful. Cough-

variant asthma may be resistant to simple dilators but a course of corticosteroids may be required.²¹

Irwin's group looked at both the immediate and long-term results of treatment.²¹ At the time of follow-up 1½ years after diagnosis, 10% of patients were still coughing. All but one of these had refused to continue their medication as they were content to know the cause of their cough and did not want to take drugs. Only one patient, whose diagnosis had been post-nasal drip, was considered a long-term treatment failure.

There is a great deal of interest in the nonspecific treatment of cough and, in fact, there are more than 100 cough preparations listed in the United States Pharmacopeia. Reassurance may be the most important treatment, though sometimes it is difficult to give until a fairly extensive workup has been completed. If patients do experience mucosal dryness, humidification or expectorants may play a role, but there is not a single study that shows a convincing role for either.³⁸ Nonetheless, like most clinicians, I use these medications on occasion in the hope of easing expectoration. Much interest has focused on antitussives,³⁹⁻⁴² but there is almost no role for their use in the treatment of chronic cough. However, during the period of recovery following a viral infection, or when a patient has a clear cause of cough for which there is no further treatment, such as radiation-induced fibrosis, they may be very helpful. Codeine in a dose of 30 to 60 mg every six to eight hours is still the apparent drug of choice, though all narcotics are effective.⁴² Administering dextromethorphan, a nonprescription narcotic derivative, is also quite efficacious though probably less so than giving codeine. Occasionally a patient, such as one we recently saw with radiation pneumonitis, may respond dramatically to oral benzonatate (Tessalon), 100 mg, three to four times a day.

Lidocaine inhaled from a nebulizer is an innovative approach to the treatment of cough. Unfortunately, reports of treatment of only several patients with chronic persistent cough are available.⁴³⁻⁴⁵ We have tried it in a few patients at a dose of 200 mg (5 ml of 4% lidocaine), lower than the recommended dose of 400 mg. We have seen only temporary relief of cough (up to 48 hours)—not the several-week response reported elsewhere.⁴³⁻⁴⁵ Another innovative approach of possible value is that of "airway rest," analogous to bowel rest for colitis. With this approach one attempts to interrupt the cough cycle with bed rest, cough suppression and sedation. Though an attractive idea, it has not been formally tested.

Conclusion

In conclusion, cough is an extraordinarily common reason for physician visits. Most coughs are related either to viral infections and are self-limited or are smoking-related. However, cough may be a cardinal and even disabling symptom of many diseases. The cause of persistent cough can usually be found by careful, if sometimes exasperatingly protracted, evaluation. Treatment is most effective when given for a specific diagnosis. However, even after the most extensive evaluation, some coughs will remain undiagnosed. In such cases, reassurance and symptomatic treatment are vital.

Questions and Answers

HOMER BOUSHEY, MD: *I wonder whether it is really helpful to diagnose as asthma the combination of cough and increased*

bronchial reactivity. The main point of measuring airway responsiveness is to identify which patients with cough may obtain relief from antiasthmatic medications. As for the patient you presented, I would like to know your actual thoughts as to the cause of cough. Do you think there are cough receptors in the distal esophagus, or do you think she was actually aspirating gastric acid?

DR STULBARG: I know you have been interested in the role of gastric reflux in the development of asthma in some patients, so I am glad you brought this up. According to some reports, this occurs by aspiration,⁴⁶ but actual documentation that that is what occurs is limited.⁴⁷ Since you are our resident expert on bronchial reactivity, I would like to throw the question back in your lap. How do you think cough occurs in patients with esophagitis?

DR BOUSHEY: *We have been interested in this problem for some time and have examined the possibility of a reflex causing bronchoconstriction in six patients who had both asthma and esophageal reflux and who reported that their asthma worsened when heartburn developed. We instilled saline or diluted hydrochloric acid into the distal esophagus and measured airway resistance. Neither solution had a measurable effect, even when the symptoms of heartburn were provoked. These negative results in a few subjects do not, of course, exclude the possibility of such a reflex, but my own suspicion is that small amounts of gastric material are being aspirated.*

DR STULBARG: In defense of the concept of recurrent aspiration in this case, this woman did give a history compatible with repeated bouts of aspiration. She recalled many episodes of choking, occurring day and night, sometimes awakening her from sleep.

WARREN GOLD, MD: **The research group here that is interested in airway function has been able to show even in asthmatic subjects that specific stimuli may cause cough without causing contraction of airway smooth muscle. The emphasis in your presentation that cough may often be a manifestation of asthma ought perhaps to be modified. In fact, people who present with intractable cough but without other airway stimuli in the environment may be different from patients with typical asthma.*

DR STULBARG: I think you are referring to the excellent research that has been done here on cough by Dean Sheppard and associates. It is known that inhaling distilled water has a very potent irritating effect on people with asthma and, in fact, will cause both cough and bronchoconstriction. The group here has shown that cough and bronchoconstriction can be separated.^{48,49} It has generally been believed that the reason asthma causes cough is that the bronchoconstriction causes deformation of the irritant receptors, resulting in cough. The work done here shows that that is not always the case. When subjects inhaled a bronchodilator before inhaling the distilled water, the bronchoconstriction but not the cough was prevented. In a separate study they showed that if subjects inhaled lidocaine before inhaling the distilled water, the cough but not the bronchoconstriction was prevented. So these studies showed very clearly the separation of cough and

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bronchoconstriction. How this relates to patients with cough and bronchial hyperreactivity, I am not sure.

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